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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 28	CA/CAplus patent coverage enhanced
NEWS 3	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 4	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 5	JUL 28	STN Viewer performance improved
NEWS 6	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 7	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 8	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 9	AUG 15	CAplus currency for Korean patents enhanced
NEWS 10	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information
NEWS 11	SEP 18	Support for STN Express, Versions 6.01 and earlier, to be discontinued
NEWS 12	SEP 25	CA/CAplus current-awareness alert options enhanced to accommodate supplemental CAS indexing of exemplified prophetic substances
NEWS 13	SEP 26	WPIDS, WPINDEX, and WPIX coverage of Chinese and and Korean patents enhanced
NEWS 14	SEP 29	IFICLS enhanced with new super search field
NEWS 15	SEP 29	EMBASE and EMBAL enhanced with new search and display fields
NEWS 16	SEP 30	CAS patent coverage enhanced to include exemplified prophetic substances identified in new Japanese-language patents
NEWS 17	OCT 07	EPFULL enhanced with full implementation of EPC2000
NEWS 18	OCT 07	Multiple databases enhanced for more flexible patent number searching
NEWS 19	OCT 22	Current-awareness alert (SDI) setup and editing enhanced
NEWS 20	OCT 22	WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 21	OCT 24	CHEMLIST enhanced with intermediate list of pre-registered REACH substances

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 17:13:18 ON 27 OCT 2008

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 26 OCT 2008 HIGHEST RN 1066603-08-4
DICTIONARY FILE UPDATES: 26 OCT 2008 HIGHEST RN 1066603-08-4

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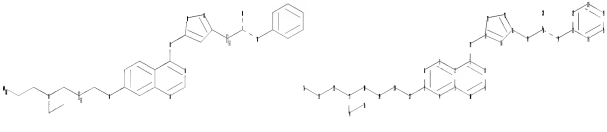

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ring nodes :
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chain bonds :

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31-32  31-34  32-33  33-36  34-35
ring bonds :
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 15-16  21-22  21-26  22-23  23-24  24-25  25-26
exact/norm bonds :
5-27  7-11  11-12  12-13  13-14  14-15  18-19  18-20  19-21  27-28  30-31  31-32
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isolated ring systems :
containing 1 : 12 : 21 :


Match level :
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L1      STRUCTURE UPLOADED

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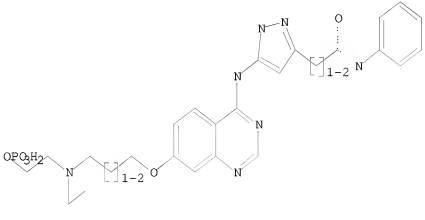


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Structure attributes must be viewed using STN Express query preparation.


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FULL SCREEN SEARCH COMPLETED -       72 TO ITERATE

100.0% PROCESSED       72 ITERATIONS                                32 ANSWERS
SEARCH TIME: 00.00.01

L2            32 SEA SSS FUL L1
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                   178.82     179.03

FILE 'CAPLUS' ENTERED AT 17:14:40 ON 27 OCT 2008
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FILE COVERS 1907 - 27 Oct 2008  VOL 149 ISS 18
FILE LAST UPDATED: 26 Oct 2008  (20081026/ED)

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reclassification data for the second quarter of 2008.

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They are available for your review at:

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=> s l2
L3          15 L2

=> d l3 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L3   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2008:771165  CAPLUS
DOCUMENT NUMBER:         149:102715
TITLE:                   Methods of treating cancer using IGF1R inhibitors
INVENTOR(S):             Wang, Yan; Zong, Chen; Seidel-Dugan, Cynthia; Wang,
                         Yaolin; Yao, Siu-Long; Lu, Brian Der-Hua; Ladha,
                         Mohamed H.
PATENT ASSIGNEE(S):      Schering Corporation, USA
SOURCE:                  PCT Int. Appl., 103pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2008076278        A2    20080626    WO 2007-US25398        20071211
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
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KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2006-874589P	P	20061213
US 2006-870937P	P	20061220
US 2007-946011P	P	20070625
US 2007-979274P	P	20071011

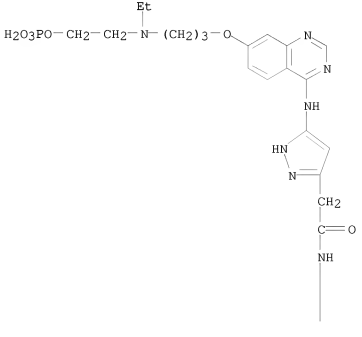
AB The present invention provides IGF1R inhibitors and combinations thereof that are effective at treating or preventing cancer. More specifically the IGF1R inhibitors are pyrrolo[2,3-d]pyrimidine derivs. or antibodies. The IGF1R inhibitors can be used in combination with other anticancer therapies, antiemetic agents, antianemic agents, or antimucositis agents.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; methods of treating cancer using IGF1R inhibitors)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A

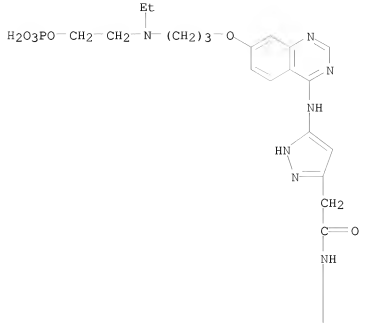


L3 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:615397 CAPLUS
DOCUMENT NUMBER: 149:26967
TITLE: Enhancement of radiation response in p53-deficient cancer cells by the Aurora-B kinase inhibitor AZD1152
AUTHOR(S): Tao, Y.; Zhang, P.; Girdler, F.; Frascogna, V.; Castedo, M.; Bourhis, J.; Kroemer, G.; Deutsch, E.
CORPORATE SOURCE: Laboratory UPRES EA27-10 Radiosensitivity of Tumors and Normal Tissues, Villejuif, Fr.
SOURCE: Oncogene (2008), 27(23), 3244-3255
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Overexpression of the Aurora-B kinase correlates with oncogenic transformation and poor prognosis. We evaluated the effects of the bona fide Aurora-B kinase inhibitor AZD1152 on tumor responses to ionizing radiation (IR). When p53wt HCT116 and A549 cells were pretreated with AZD1152-HQPA prior to IR, additive effects were observed Interestingly, more pronounced tumoricidal effects were observed in p53-deficient HCT116 and HT29 cells, as well as A549 cells treated with the p53 inhibitor cyclic pifithrin-α. In vivo studies on xenografted mice confirmed enhanced tumor growth delay after the combination of IR plus AZD1152-IR as compared to IR alone. Again, this effect was more pronounced with p53-/- HCT116 and p53-mutant xenografts. The AZD1152-mediated radiosensitization was mimicked by knockdown of Aurora-B with a short interference RNA or by inhibition of Aurora-B by transfection with an inducible kinase-dead Aurora-B. The radiosensitizing effect of AZD1152 was lost in CHK2-/- and 14-3-3-/- HCT116 cells. Altogether, these data indicate that AZD1152 can radiosensitize tumor cell lines in vitro and in vivo, the fact that these effects are exacerbated in p53-deficient cancer cells is of potential interest for further clin. development.

IT 722543-31-9, AZD1152
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of radiotherapy response in p53-deficient cancer cells by Aurora-B kinase inhibitor AZD1152)
RN 722543-31-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:331285 CAPLUS
DOCUMENT NUMBER: 148:486547
TITLE: Preclinical evaluation of M30 and M65 ELISAs as biomarkers of drug induced tumor cell death and antitumor activity
AUTHOR(S): Cummings, Jeffrey; Hodgkinson, Cassandra; Odedra, Rajesh; Sini, Patrizia; Heaton, Simon P.; Mundt, Kirsten E.; Ward, Tim H.; Wilkinson, Robert W.; Growcott, Jim; Hughes, Andrew; Dive, Caroline
CORPORATE SOURCE: Clinical and Experimental Pharmacology, Paterson Institute for Cancer Research, University of Manchester, Manchester, UK
SOURCE: Molecular Cancer Therapeutics (2008), 7(3), 455-463 CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB M30 and M65 are ELISAs that detect different circulating forms of

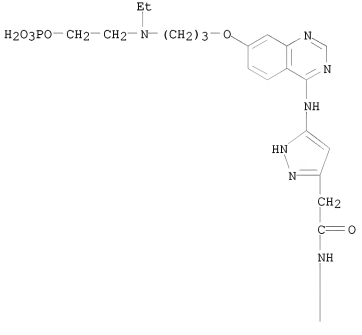
cytokeratin 18. Using the aurora kinase inhibitor AZD1152 and the SW620 human colon cancer xenograft, expts. were conducted to qualify preclinically both assays as serol. biomarkers of cell death. Using two different apoptotic markers, the kinetics of cell death induced by AZD1152 was first characterized in vitro in three different cell lines and shown to peak 5 to 7 days after drug addition Treatment of non-tumor-bearing rats with AZD1152 (25 mg/kg) produced no alterations in circulating baseline values of M30 and M65 antigens. In treated, tumor-bearing animals, M30 detected a 2- to 3-fold ($P < 0.05$) increase in plasma antigen levels by day 5 compared with controls. This correlated to a 3-fold increase in the number of apoptotic cells detected on day 5 in SW620 xenografts using immunohistochem. By contrast, M65 did not detect a drug-induced increase in circulating antigen levels at day 5. However, M65 plasma levels correlated to changes in tumor growth in control animals ($r2 = 0.93$; $P < 0.01$) and also followed the magnitude of the temporal effect of AZD1152 on tumor growth. An intermediate but active dose of AZD1152 (12.5 mg/kg) produced a less significant increase in M30 plasma levels at day 5. It was also confirmed that the plasma profiles of M30 and M65 mirrored closely those measured in whole tumor lyzates. We conclude that M30 is a pharmacodynamic biomarker of AZD1152-induced apoptosis in the SW620 xenograft model, whereas M65 is a biomarker of therapeutic response.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preclin. evaluation of M30 and M65 ELISAs as biomarkers of drug induced tumor cell death and antitumor activity)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



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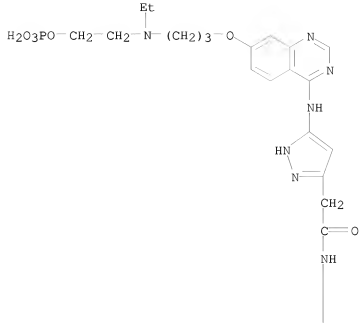
L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:232751 CAPLUS
DOCUMENT NUMBER: 148:417468
TITLE: The selective Aurora B kinase inhibitor AZD1152 is a potential new treatment for multiple myeloma
AUTHOR(S): Evans, Robert P.; Naber, Claudia; Steffler, Tara; Checkland, Tamara; Maxwell, Christopher A.; Keats, Jonathan J.; Belch, Andrew R.; Pilarski, Linda M.; Lai, Raymond; Reiman, Tony
CORPORATE SOURCE: Department of Oncology, University of Alberta/Cross Cancer Institute, Edmonton, AB, Can.
SOURCE: British Journal of Haematology (2008), 140(3), 295-302 CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aurora kinases are potential targets for cancer therapy. Previous studies have validated Aurora kinase A as a therapeutic target in multiple myeloma (MM), and have demonstrated in vitro anti-myeloma effects of small mol. Aurora kinase inhibitors that inhibit both Aurora A and B. This study demonstrated that Aurora B kinase was strongly expressed in myeloma cell lines and primary plasma cells. The selective Aurora B inhibitor AZD1152-induced apoptotic death in myeloma cell lines at nanomolar concns., with a cell cycle phenotype consistent with that reported previously for Aurora B inhibition. In some cases, AZD1152 in combination with dexamethasone showed increased anti-myeloma activity compared with the use of either agent alone. AZD1152 was active against sorted CD138+ BM plasma cells from myeloma patients but also, as expected, was toxic to CD138- marrow cells from the same patients. In a murine myeloma xenograft model, AZD1152-inhibited tumor growth at well-tolerated doses and induced cell death in established tumors, with associated mild, transient leucopenia. AZD1152 shows promise in these preclin. studies as a novel treatment for MM.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Aurora kinase B inhibitor AZD1152 induced apoptosis in myeloma cell, alone or combined with dexamethasone reduced viability of patient bone marrow plasma cell and inhibited tumor growth in myeloma xenografted mouse)

RN 722543-31-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:210298 CAPLUS
DOCUMENT NUMBER: 148:393556
TITLE: Emerging role of Aurora kinase inhibitors in chronic myeloid leukemia
AUTHOR(S): Alvarado, Yesid; Cortes, Jorge E.
CORPORATE SOURCE: Department of Leukemia, M. D. Anderson Cancer Center, University of Texas, Houston, USA
SOURCE: Clinical Leukemia (2007), 1(6), 325-330
CODEN: CLLEAW; ISSN: 1931-6925
PUBLISHER: CIG Media Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Resistance to imatinib and second-generation tyrosine kinase inhibitors is an ongoing problem most frequently mediated through mutations of the Bcr-Abl kinase domain. One mutation that affects responsiveness to all current available agents is T315I. Aurora proteins belong to a small family of serine/threonine kinases that are essential for proliferating cells and have been identified as key regulators of

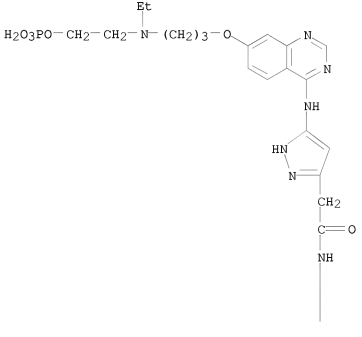
different steps in mitosis and meiosis, ranging from the formation of the mitotic spindle up to cytokinesis. Unexpectedly, Aurora kinase inhibitors have been found to have activity against the T315I bcr-abl mutation, and some of them might rise as important therapeutic options. The common mechanism of action for protein kinase inhibition is competition with ATP for the active site-binding pocket, which is very similar among the protein kinases, and this could explain the cross-reactivity. Herein, we discuss the basics of imatinib resistance development and Aurora kinase biol., and describe a selected group of Aurora kinase inhibitors with potential activity in this patient population.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib resistance mediated through bcr-abl gene may be prevented by Aurora kinase inhibitors including AZD-1152 in patient with chronic myeloid leukemia)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:68932 CAPLUS
DOCUMENT NUMBER: 148:168706
TITLE: 3-Benzoylamino-1H-pyrazole-4-carboxamides as CDK kinase inhibitors, and their preparation, pharmaceutical combinations and use in the treatment of proliferative diseases
INVENTOR(S): Lyons, John Francis; Squires, Matthew Simon; Thompson, Neil Thomas; Gallagher, Neil James; Curry, Jayne Elizabeth
PATENT ASSIGNEE(S): Astex Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 191pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008007113	A2	20080117	WO 2007-GB2640	20070713

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-831043P P 20060714
OTHER SOURCE(S): MARPAT 148:168706
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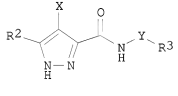

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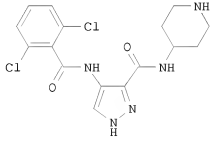


II

AB The invention provides a combination comprising an ancillary compound and a compound having the formula I: or salts or tautomers or N-oxides or solvates thereof/. Compds. of formula I wherein X is 5- to 6-membered (hetero/carbo)cyclic ring, amino, acylamino,sulfonylamino, etc.; Y is a bond and C1-3 alkylene; R2 is H, halo, C1-4 alkoxy, (un)substituted C1-4 hydrocarbyl; R3 is H, 3- to 12-membered (hetero/carbo)cyclic group; and their salts, tautomers, N-oxides and solvates thereof, are claimed.

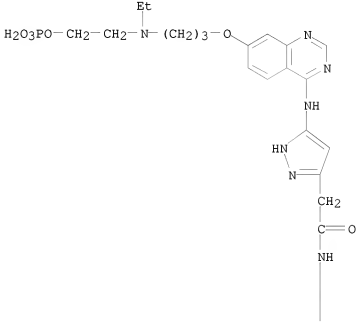
Example compound II•MsOH was prepared by esterification of 4-nitropyrazole-3-carboxylic acid; the resulting 4-nitropyrazole-3-carboxylic acid Me ester underwent hydrogenation to give 4-aminopyrazole-3-carboxylic acid Me ester, which underwent amidation with 2,6-dichlorobenzoyl chloride to give 4-(2,6-dichlorobenzoylamino)pyrazole-3-carboxylic acid Me ester, which underwent hydrolysis to give 4-(2,6-dichlorobenzoylamino)pyrazole-3-carboxylic acid, which underwent chlorination to give the corresponding acid chloride, which underwent amidation with 4-amino-1-Boc-piperidine to give 1-Boc-piperidin-4-yl 4-(2,6-dichlorobenzoylamino)pyrazole-3-carboxamide, which underwent hydrolysis to give compound II•MsOH. All the invention compds. were evaluated for their CDK kinase inhibitory activity (some data given).

IT 722543-31-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of benzoylaminopyrazolecarboxamides as CDK kinase inhibitors useful in the treatment of proliferative diseases)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:43490 CAPLUS
DOCUMENT NUMBER: 148:135980
TITLE: Blood levels of insulin-like growth factor-binding protein 2 as a marker for monitoring the effectiveness of inhibitors of insulin-like growth factor I receptors in cancer therapy
INVENTOR(S): Wang, Yan
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 133pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008005469	A2	20080110	WO 2007-US15423	20070629
WO 2008005469	A3	20080228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20080112888	A1	20080515	US 2007-771454	20070629

PRIORITY APPLN. INFO.: US 2006-818004P P 20060630

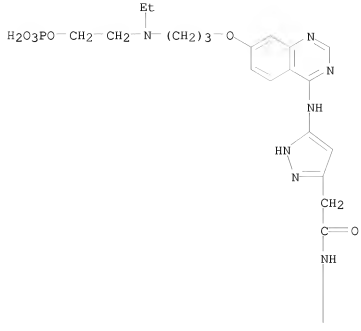
AB The present invention provides method for quickly and conveniently determining if a given treatment regimen of insulin-like growth factor I receptor (IGF1R) inhibitor is sufficient, e.g., to saturate IGF1 R receptors in the body of a subject. Blood levels of insulin-like growth factor-binding protein 2 (IGFBP2) are shown to be strongly correlated with the effectiveness of IGF1R receptor therapy. Several clin. relevant detns. may be made based on this point, including, for example, whether the dosage of the regimen is sufficient or should be increased. The relationship is demonstrated using animal xenograft models of neuroblastoma. Treatment with monoclonal antibodies to IGFR1 lowered the blood levels of IGFBP2. The level of IGFBP2 correlated with the tumor size.

IT 722543-31-9, AZD 1152
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy using; blood levels of IGBP2 as marker for monitoring effectiveness of inhibitors of IGF1 receptors in cancer therapy)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1334468 CAPLUS
DOCUMENT NUMBER: 148:11256
TITLE: Quinazolin-4-ylaminopyrazolecarboxamides as aurora kinase inhibitors useful in bombination therapy for the treatment of cancer and their preparation
INVENTOR(S): Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 39pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007132215	A1	20071122	WO 2007-GB1754	20070514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,

KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: GB 2006-9619 A 20060516
OTHER SOURCE(S): MARPAT 148:11256
GI

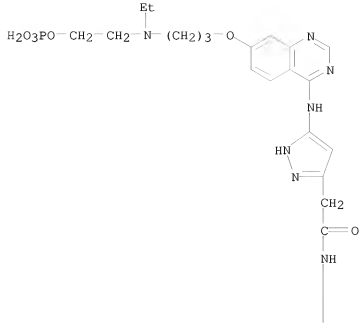
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A combination comprising an aurora kinase inhibitor and an efflux transporter inhibitor wherein the aurora kinase inhibitor is a compound of formula I or pharmaceutically acceptable salt thereof for use in the treatment of hyperproliferative diseases such as cancer. Compds. of formula I wherein n is 0, 1, 2 and 3; R1 is C1-4 hydroxyalkyl and C1-4 phosphonooxyalkyl; R2 is H, C1-4 (hydroxy)alkyl, C1-4 alkoxy-C1-4 alkyl, and heterocyclyl; R1R2 together with nitrogen form a (un)substituted 4- to 6-membered heterocyclic ring; R3 is H and C1-4 alkoxy; R4, R6 and R6 are independently H and C1-4 alkyl; R5 is (un)substituted aryl; and their pharmaceutically acceptable salts thereof. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their aurora kinase inhibitory activity (some data given).

IT 722543-31-9P 722543-50-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolineaminopyrazolecarboxamides for combination therapy of hyperproliferative diseases including cancer using aurora kinase inhibitors and an efflux transporter inhibitors)

RN 722543-31-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

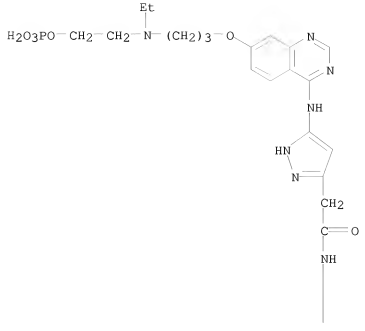
PAGE 1-A



PAGE 2-A

RN 722543-50-2 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

●2 HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1334419 CAPLUS
DOCUMENT NUMBER: 147:548107
TITLE: Maleate co-crystal of AZD 1152 for dosage forms for treatment of hyperproliferative diseases
INVENTOR(S): Sependa, George Joseph; Storey, Richard
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 50pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2007132227	A1	20071122	WO 2007-GB1771	20070514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20080045481	A1	20080221	US 2007-748651	20070515

PRIORITY APPLN. INFO.: GB 2006-9621 A 20060516

AB The present invention relates to a novel co-crystal form of 2-{ethyl[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxo-ethyl}-1H-pyrazol-3-yl)amino]quinazolin-7-yl}oxy)propyl]amino} Et dihydrogen phosphate (AZD 1152), an aurora kinase inhibitor useful in the treatment of hyperproliferative diseases, such as cancer. More specifically, the invention relates to a maleate co-crystal of AZD 1152, to a process for its preparation, its use in the manufacturing of a medicament for the treatment of hyperproliferative diseases, and to methods of treating hyperproliferative diseases by administering a therapeutically effective amount of a maleate co-crystal of AZD 1152. A particular crystalline form of a maleate co-crystal of AZD 1152 is also described. Thus, crude AZD 1152 (preparation given, estimated at 7.44 g @ 100%, 11.61 mM) was added to DMSO (36 mL) and left at ambient temperature to produce a pale brown solution To this solution was added a solution of maleic acid (1.76 g, 15.16 mM, 1.31 mol equivalent) in MeOH (36 mL) and the mixture left to stand overnight at ambient temperature Next day an aliquot of the clear solution was transferred to a vial, scratched and left sealed for several hours. A deposit of white solid formed and this was transferred to the flask and left to stir. Gradually the solution turned turbid and solid deposited. The slurry was left to settle for several days and finally filtered. The cake was washed with a 1:1 mixture of DMSO/MeOH, slurried in situ with MeOH and then dried in vacuo. NMR confirmed the solid to be the maleate co-crystal of AZD1152 (yield of about 78.7%).

IT 957104-91-5P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of maleate co-crystal of AZD 1152 for dosage forms for treatment of hyperproliferative diseases)

RN 957104-91-5 CAPLUS

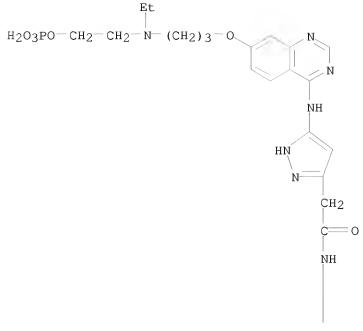
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 722543-31-9

CMF C26 H31 F N7 O6 P

PAGE 1-A

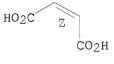


PAGE 2-A

CM 2

CRN 110-16-7
CMF C4 H4 O4

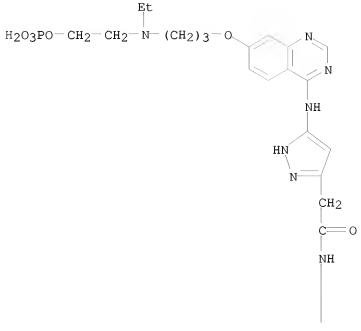
Double bond geometry as shown.



IT 722543-31-9P, AZD 1152
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of maleate co-crystal of AZD 1152 for dosage forms for treatment of hyperproliferative diseases)
RN 722543-31-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-

fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1300709 CAPLUS
DOCUMENT NUMBER: 147:522230
TITLE: Pharmaceutical combinations of diazole derivatives for cancer treatment and their preparation
INVENTOR(S): Squires, Matthew Simon
PATENT ASSIGNEE(S): Astex Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 254pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007129062	A1	20071115	WO 2007-GB1640	20070504

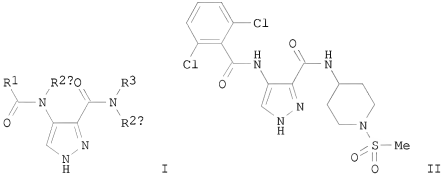
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-746694P P 20060508
US 2006-830966P P 20060714

OTHER SOURCE(S): MARPAT 147:522230

GI



AB The invention provides a combination comprising (or consisting essentially of) an ancillary compound and a compound of the formula I, or salts, tautomers, solvates and N-oxides thereof. The combinations have activity as inhibitors of CDK kinases and inhibit the proliferation of cancer cells. Compds. of formula I wherein, R1 is 2,6-dichlorophenyl; R2a and R2b are both H; R3 is C1-4 alkyl-SO2-piperidinyl; and their salts, tautomers, solvates, and N-oxides thereof, are claimed. Example compound II was prepared by methylation of 4-nitropyrazole-3-carboxylic acid; the resulting 4-nitropyrazole-3-carboxylic acid Me ester underwent hydrogenation to give 4-aminopyrazole-3-carboxylic acid Me ester, which underwent acylation with 2,6-dichlorobenzoyl chloride followed by hydrolysis to give 4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carboxylic acid, which underwent amidation with 4-amino-1-Boc-piperidine, to give 4-[[4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carbonyl]amino]piperidine-1-carboxylic acid tert-Bu ester, which underwent hydrolysis to give 4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carboxylic acid piperidin-4-yl amide hydrochloride, which underwent sulfonylation with methanesulfonyl chloride to give compound II. The crystal structure of compound II was also determined The invention compds. were evaluated for their CDK kinase inhibitory activity (some data given).

IT 722543-31-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

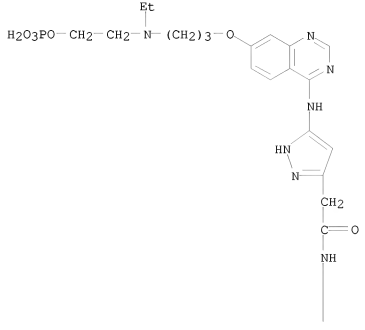
(preparation of pyrazole derivs. and their pharmaceutical compns. as CDK kinase inhibitors useful in treatment and prophylaxis of cancer)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-

(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1050775 CAPLUS

DOCUMENT NUMBER: 148:321846

TITLE: AZD1152, a novel and selective aurora B kinase inhibitor, induces growth arrest, apoptosis, and sensitization for tubulin depolymerizing agent or topoisomerase II inhibitor in human acute leukemia cells in vitro and in vivo

AUTHOR(S): Yang, Jing; Ikezoe, Takayuki; Nishioka, Chie; Tasaka, Taizo; Taniguchi, Ayuko; Kuwayama, Yoshio; Komatsu, Naoki; Bandobashi, Kentaro; Togitani, Kazuto; Koeffler, H. Phillip; Taguchi, Hirokuni; Yokoyama, Akihito

CORPORATE SOURCE: Department of Hematology and Respiratory Medicine, Kochi University, Nankoku, Kochi, Japan

SOURCE: Blood (2007), 110(6), 2034-2040

CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

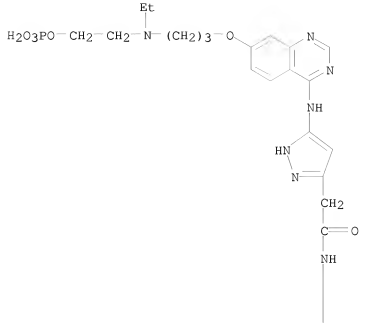
AB Aurora kinases play an important role in chromosome alignment, segregation, and cytokinesis during mitosis. We have recently shown that hematopoietic malignant cells including those from acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) aberrantly expressed Aurora A and B kinases, and ZM447439, a potent inhibitor of Aurora kinases, effectively induced growth arrest and apoptosis of a variety of leukemia cells. The present study explored the effect of AZD1152, a highly selective inhibitor of Aurora B kinase, on various types of human leukemia cells. AZD1152 inhibited the proliferation of AML lines (HL-60, NB4, MOLM13), ALL line (PALL-2), biphenotypic leukemia (MV4-11), acute eosinophilic leukemia (EOL-1), and the blast crisis of chronic myeloid leukemia K562 cells with an IC50 ranging from 3 nM to 40 nM, as measured by thymidine uptake on day 2 of culture. These cells had 4N/8N DNA content followed by apoptosis, as measured by cell-cycle anal. and annexin V staining, resp. Of note, AZD1152 synergistically enhanced the antiproliferative activity of vincristine, a tubulin depolymg. agent, and daunorubicin, a topoisomerase II inhibitor, against the MOLM13 and PALL-2 cells in vitro. Furthermore, AZD1152 potentiated the action of vincristine and daunorubicin in a MOLM13 murine xenograft model. Taken together, AZD1152 is a promising new agent for treatment of individuals with leukemia. The combined administration of AZD1152 and conventional chemotherapeutic agent to patients with leukemia warrants further investigation.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AZD1152 induces growth arrest, apoptosis, and sensitization for tubulin depolymg. agent or topoisomerase II inhibitor in human acute leukemia cells)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:654991 CAPLUS
DOCUMENT NUMBER: 147:377849
TITLE: AZD1152, a Selective Inhibitor of Aurora B Kinase, Inhibits Human Tumor Xenograft Growth by Inducing Apoptosis
AUTHOR(S): Wilkinson, Robert W.; Odedra, Rajesh; Heaton, Simon P.; Wedge, Stephen R.; Keen, Nicholas J.; Crafter, Claire; Foster, John R.; Brady, Madeleine C.; Bigley, Alison; Brown, Elaine; Byth, Kate F.; Barrass, Nigel C.; Mundt, Kirsten E.; Foote, Kevin M.; Heron, Nicola M.; Jung, Frederic H.; Mortlock, Andrew A.; Boyle, F. Thomas; Green, Stephen
CORPORATE SOURCE: AstraZeneca Pharmaceuticals, Macclesfield, Cheshire, UK
SOURCE: Clinical Cancer Research (2007), 13(12), 3682-3688
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal

LANGUAGE: English

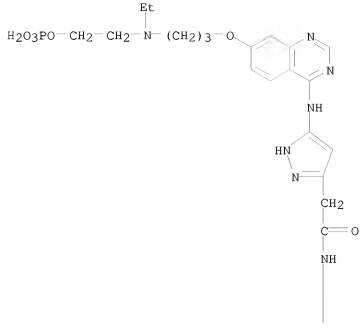
AB PURPOSE: In the current study, we examined the in vivo effects of AZD1152, a novel and specific inhibitor of Aurora kinase activity (with selectivity for Aurora B). Exptl. DESIGN: The pharmacodynamic effects and efficacy of AZD1152 were determined in a panel of human tumor xenograft models. AZD1152 was dosed via several parenteral (s.c. osmotic mini-pump, i.p., and i.v.) routes. RESULTS: AZD1152 potently inhibited the growth of human colon, lung, and hematol. tumor xenografts (mean tumor growth inhibition range, 55% to ≥100%; $P < 0.05$) in immunodeficient mice. Detailed pharmacodynamic anal. in colorectal SW620 tumor-bearing athymic rats treated i.v. with AZD1152 revealed a temporal sequence of phenotypic events in tumors: transient suppression of histone H3 phosphorylation followed by accumulation of 4N DNA in cells (2.4-fold higher compared with controls) and then an increased proportion of polyploid cells (>4N DNA, 2.3-fold higher compared with controls). Histol. anal. showed aberrant cell division that was concurrent with an increase in apoptosis in AZD1152-treated tumors. Bone marrow analyses revealed transient myelosuppression with the drug that was fully reversible following cessation of AZD1152 treatment. CONCLUSIONS: These data suggest that selective targeting of Aurora B kinase may be a promising therapeutic approach for the treatment of a range of malignancies. In addition to the suppression of histone H3 phosphorylation, determination of tumor cell polyploidy and apoptosis may be useful biomarkers for this class of therapeutic agent. AZD1152 is currently in phase I trials.

IT 722543-31-9, AZD 1152
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AZD1152 inhibited human tumor xenograft growth and induced apoptosis in colorectal SW620 tumor-bearing athymic rat)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:561763 CAPLUS
DOCUMENT NUMBER: 146:494108
TITLE: Anti-angiogenic activity of 2-methoxyestradiol in combination with anti-cancer agents
INVENTOR(S): Plum, Stacy M.; Strawn, Steven J.; Lavallee, Theresa M.; Sidor, Carolyn F.; Fogler, William E.; Treston, Anthony M.
PATENT ASSIGNEE(S): Entremed, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007059111	A2	20070524	WO 2006-US44152	20061114

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20070185069 A1 20070809 US 2006-599997 20061114

PRIORITY APPLN. INFO.: US 2005-736220P P 20051114

US 2006-788354P P 20060331

AB The present invention relates generally to methods and compns. of treating disease characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering antiangiogenic agents in combination with chemotherapeutic agents. More specifically, the present invention relates to a methods and compns. of treating diseases characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering 2-methoxyestradiol, in combination with chemotherapeutic agents.

IT 722543-31-9

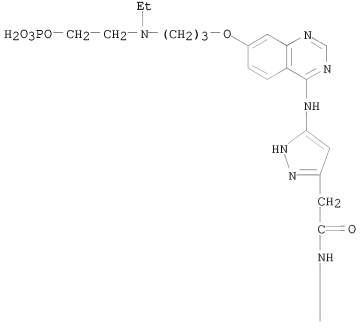
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anti-angiogenic activity of 2-methoxyestradiol and other estradiols in combination with anti-cancer agents)

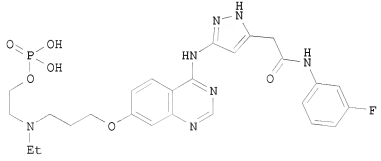
RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:321162 CAPLUS
DOCUMENT NUMBER: 146:521755
TITLE: Discovery, Synthesis, and in Vivo Activity of a New Class of Pyrazolylamino Quinazolines as Selective Inhibitors of Aurora B Kinase
AUTHOR(S): Mortlock, Andrew A.; Foote, Kevin M.; Heron, Nicola M.; Jung, Frederic H.; Pasquet, Georges; Lohmann, Jean-Jacques M.; Warin, Nicolas; Renaud, Fabrice; De Savi, Chris; Roberts, Nicola J.; Johnson, Trevor; Dousson, Cyril B.; Hill, George B.; Perkins, David; Hatter, Glenn; Wilkinson, Robert W.; Wedge, Stephen R.; Heaton, Simon P.; Odedra, Rajesh; Keen, Nicholas J.; Crafter, Claire; Brown, Elaine; Thompson, Katherine; Brightwell, Stephen; Khatri, Liz; Brady, Madeleine C.; Kearney, Sarah; McKillop, David; Rhead, Steve; Parry, Tony; Green, Stephen
CORPORATE SOURCE: AstraZeneca Pharmaceuticals, Macclesfield, Cheshire, SK10 4TG, UK
SOURCE: Journal of Medicinal Chemistry (2007), 50(9), 2213-2224
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:521755
GI



I

AB A series of pyrazolylamino-substituted quinazolines was synthesized and biol. evaluated as inhibitors of Aurora kinases, which have been the subject of considerable interest as targets for the development of new anticancer agents. Some of the products demonstrated greater than 1000-fold selectivity for Aurora B over Aurora A kinase activity in

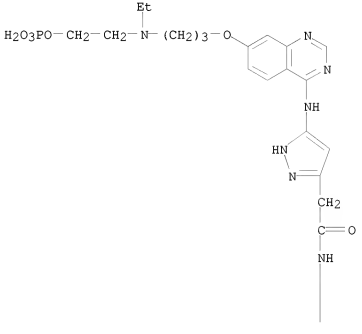
recombinant enzyme assays. These compds. have been designed for parenteral administration and achieve high levels of solubility by virtue of their ability to be delivered as readily activated phosphate derivs. The prodrugs are comprehensively converted to the des-phosphate form in vivo, and the active species have advantageous pharmacokinetic properties and safety pharmacol. profiles. The compds. display striking in vivo activity, and I (AZD1152) has been selected for clin. evaluation and is currently in phase 1 clin. trials.

IT 722543-31-9P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(AZD 1152, solubility; synthesis and in vivo activity of pyrazolylamino-substituted quinazolines as selective inhibitors of Aurora B kinase and antitumor agents)

RN 722543-31-9 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

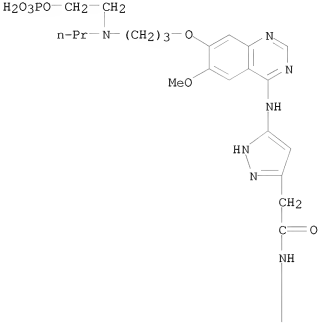
IT 722542-97-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP

(Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solubility; synthesis and in vivo activity of pyrazolylamino-substituted quinazolines as selective inhibitors of Aurora B kinase and antitumor agents)

RN 722542-97-4 CAPLUS

CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



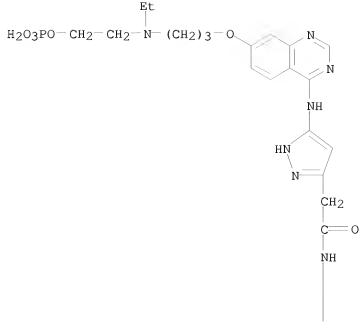
PAGE 2-A

IT 722543-50-2P 722543-78-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and in vivo activity of pyrazolylamino-substituted quinazolines as selective inhibitors of Aurora B kinase and antitumor agents)

RN 722543-50-2 CAPLUS

CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 1-A

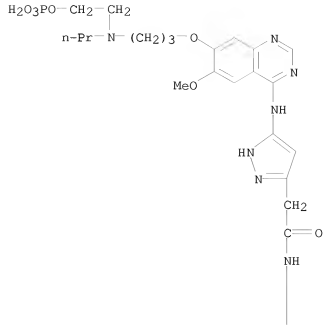


PAGE 2-A

● 2 HCl

RN 722543-78-4 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

●2 HCl

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:566624 CAPLUS
DOCUMENT NUMBER: 141:123757
TITLE: Preparation of phosphonooxy quinazoline derivatives and their pharmaceutical use
INVENTOR(S): Heron, Nicola Murdoch; Jung, Frederic Henri; Pasquet, Georges Rene; Mortlock, Andrew Austen
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058781	A1	20040715	WO 2003-GB5613	20031222
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003290313	A1	20040722	AU 2003-290313	20031222
AU 2003290313	B2	20070510		
EP 1578755	A1	20050928	EP 2003-782672	20031222
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BR 2003017717	A	20051122	BR 2003-17717	20031222
JP 2006512418	T	20060413	JP 2005-509716	20031222
CN 1764668	A	20060426	CN 2003-80109902	20031222
CN 100349906	C	20071121		
AT 370958	T	20070915	AT 2003-782672	20031222
EP 1847539	A1	20071024	EP 2007-9390	20031222
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CN 101074227	A	20071121	CN 2007-10127910	20031222
ES 2290529	T3	20080216	ES 2003-782672	20031222
NZ 540698	A	20080530	NZ 2003-540698	20031222
NO 2005002855	A	20050803	NO 2005-2855	20050613
US 20060116357	A1	20060601	US 2005-539220	20050617
IN 2005DN02718	A	20061229	IN 2005-DN2718	20050620
MX 2005PA06918	A	20050818	MX 2005-PA6918	20050623
HK 1080481	A1	20080125	HK 2006-100400	20060110
AU 2007202223	A1	20070607	AU 2007-202223	20070517
IN 2007DN04430	A	20070831	IN 2007-DN4430	20070611
JP 2007326862	A	20071220	JP 2007-169891	20070628

PRIORITY APPLN. INFO.:

EP 2002-293238	A	20021224
EP 2003-291315	A	20030602
AU 2003-290313	A3	20031222
CN 2003-80109902	A3	20031222
EP 2003-782672	A3	20031222
JP 2005-509716	A3	20031222
WO 2003-GB5613	W	20031222
IN 2005-DN2718	A3	20050620

OTHER SOURCE(S): MARPAT 141:123757

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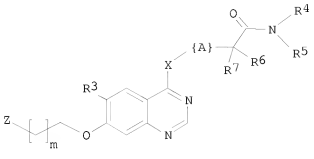

I

AB Preparation of phosphonooxy quinazoline derivs., I (A = 5-membered heteroaryl containing a nitrogen atom and one or two further nitrogen atoms; X = O, S, S(O), S(O)2, organoamino; m = 0-3; Z = organoamino, phosphonooxy, (un)substituted C3-6 cycloalkyl, etc.; R3 = H, halo, cyano, nitro, C1-6 alkoxy, C1-6 alkyl, alkoxycarbonyl, organoamido, sulfonylamido, etc.; R4 = H, C1-4 alkyl, heteroaryl, heteroaryl C1-4 alkyl, aryl, etc.; R5 = H, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, C3-6 cycloalkyl, etc.; R6, R7 = H, halo, C1-4 alkyl, C3-6 cycloalkyl, hydroxy, C1-4 alkoxy, etc.), and compns. containing them, processes for their preparation and their use in therapy is described. Thus, reaction of N-(3-fluorophenyl)-2-{3-[(7-{3-[4-(hydroxymethyl)piperidin-1-yl]propoxy}-6-methoxyquinazolin-4-yl)amino]-1H-pyrazol-5-yl}acetamide (preparation given) with di-tert-butyl-diethylphosphoramidite gave 70% di-tert-Bu {1-[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1Hpyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]piperidin-4-yl}methyl phosphate which on acidic hydrolysis gave 94% title compound, di-tert-Bu {1-[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1Hpyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]piperidin-4-yl}methyl dihydrogen phosphate. In vitro Aurora-A and Aurora-B kinase inhibition activity and cell proliferation and cycle anal. of the prepared compds. were determined

IT 722542-93-0P 722542-97-4P 722542-98-5P
722542-99-6P 722543-00-2P 722543-01-3P
722543-02-4P 722543-05-7P 722543-06-8P
722543-07-9P 722543-08-0P 722543-11-5P
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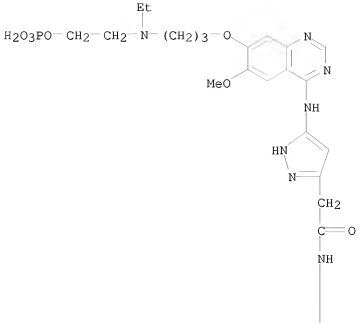
722543-33-1P 722543-36-4P 722543-37-5P
722543-38-6P 722543-42-2P 722543-46-6P
722543-47-7P 722543-50-2P 722543-53-5P
722543-56-8P 722543-57-9P 722543-62-6P
722543-78-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phosphonooxy quinazoline derivs. and their pharmaceutical use)

RN 722542-93-0 CAPLUS

CN 1H-Pyrazole-3-acetamide, N-(3,5-difluorophenyl)-5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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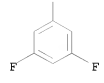
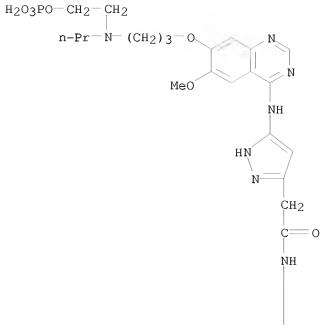


RN 722542-97-4 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

RN 722542-98-5 CAPLUS
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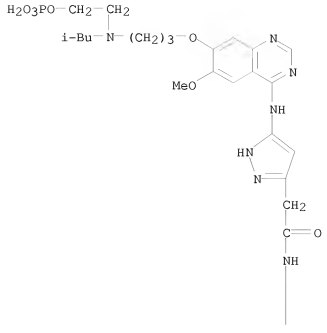

PAGE 2-A

RN 722542-99-6 CAPLUS
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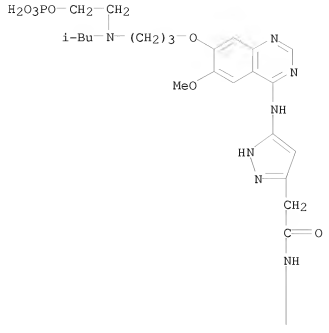
PAGE 1-A



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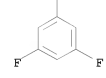
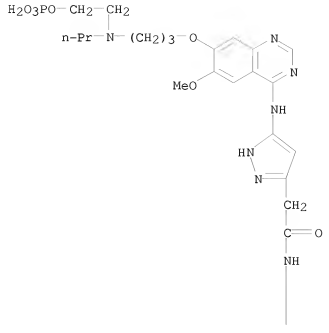


RN 722543-00-2 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(3,5-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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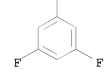

RN 722543-01-3 CAPLUS
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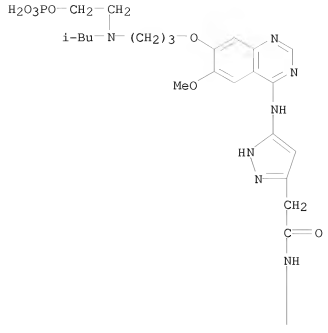
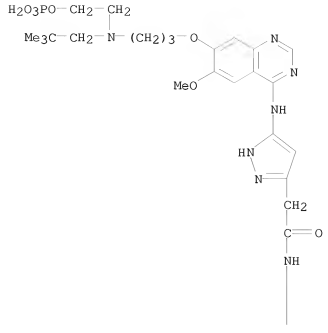
PAGE 1-A



PAGE 2-A

RN 722543-02-4 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[(2,2-dimethylpropyl)[2-(phosphonooxy)ethyl]amino]propoxy]-6-methoxy-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

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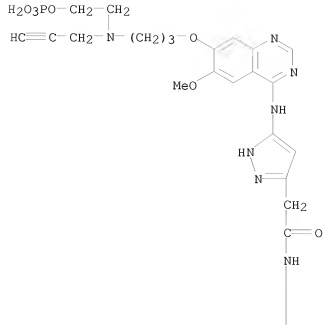
PAGE 1-A



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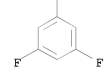
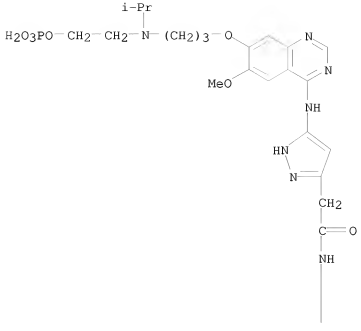


RN 722543-06-8 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[(1-methylethyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

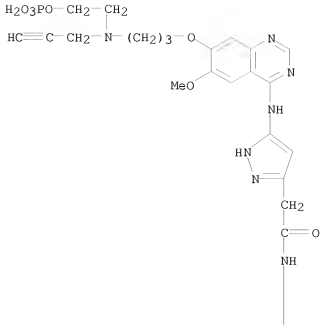
PAGE 1-A



PAGE 2-A

RN 722543-07-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]-2-propyn-1-ylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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RN 722543-08-0 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[(2-methoxyethyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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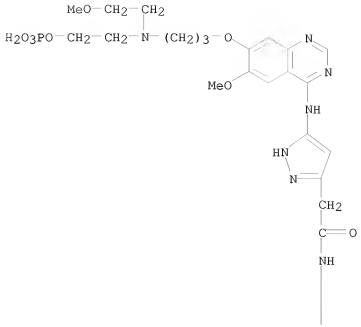

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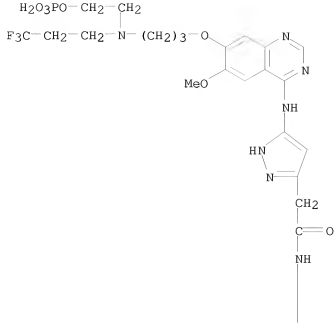
RN 722543-11-5 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(3-fluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl](3,3,3-trifluoropropyl)amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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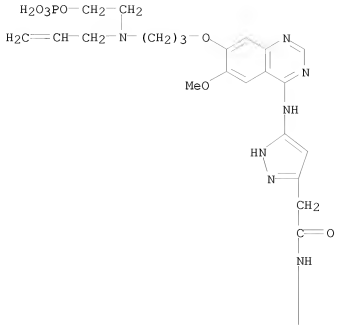
RN 722543-12-6 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]-2-propen-1-ylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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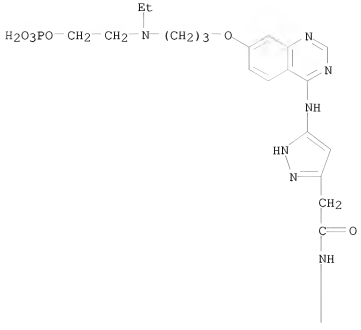
RN 722543-20-6 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

PAGE 1-A



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RN 722543-21-7 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[3-[(1-methylethyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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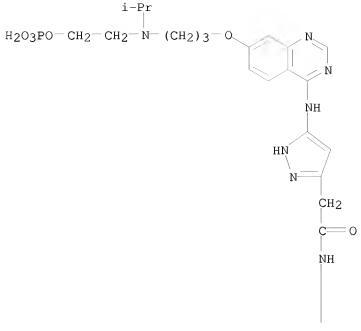

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RN 722543-25-1 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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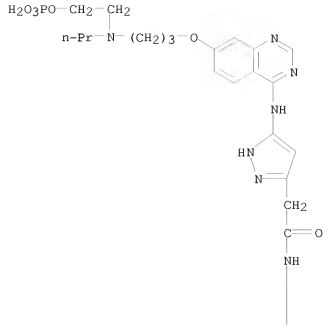

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RN 722543-26-2 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[butyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(2,3-difluorophenyl)- (CA INDEX NAME)

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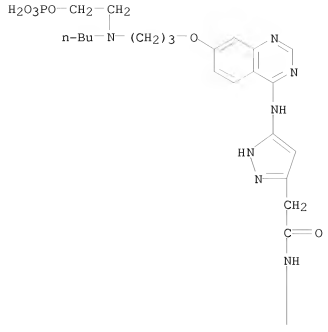

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RN 722543-31-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

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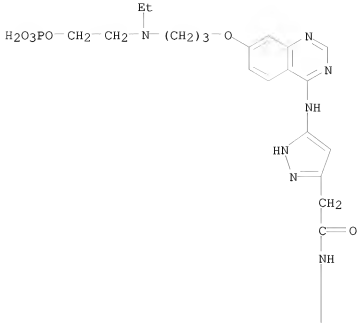

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RN 722543-33-1 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(3-fluorophenyl)-5-[[7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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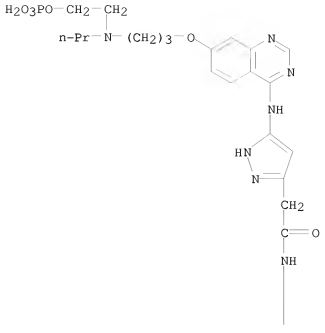

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RN 722543-36-4 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(3-fluorophenyl)-5-[[7-[3-[(2-methoxyethyl)[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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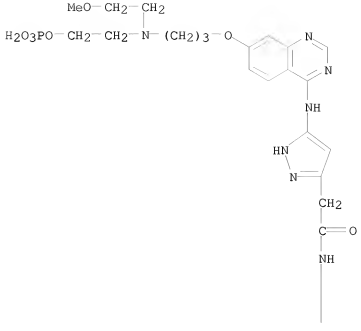

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RN 722543-37-5 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[4-[[2-(phosphonooxy)ethyl]propylamino]butoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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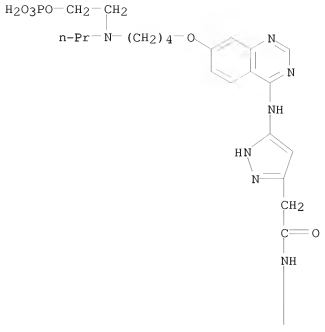

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RN 722543-38-6 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[4-[ethyl[2-(phosphonooxy)ethyl]amino]butoxy]-4-quinazolinyl]amino]- (CA INDEX NAME)

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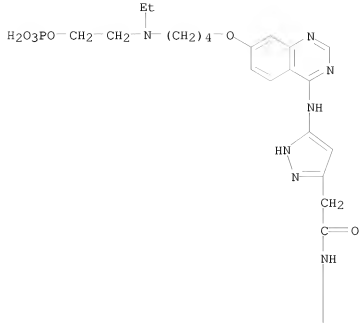

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RN 722543-42-2 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-fluoro-4-quinazolinyl]amino]-N-(3-fluorophenyl)- (CA INDEX NAME)

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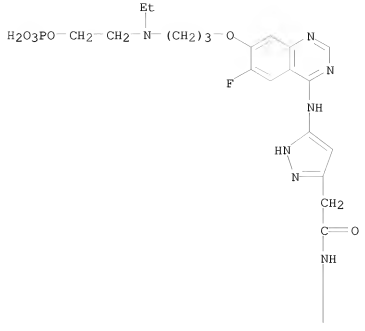

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RN 722543-46-6 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

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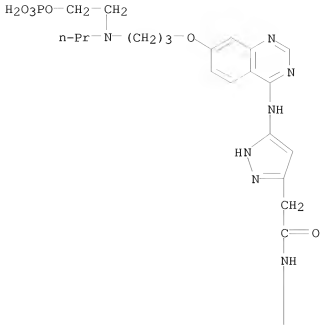

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● 2 HCl

RN 722543-47-7 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[butyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(2,3-difluorophenyl)-, hydrochloride (1:2) (CA INDEX NAME)

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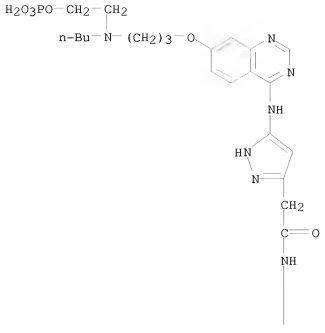

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● 2 HCl

RN 722543-50-2 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-4-quinazolinyl]amino]-N-(3-fluorophenyl)-, hydrochloride (1:2) (CA INDEX NAME)

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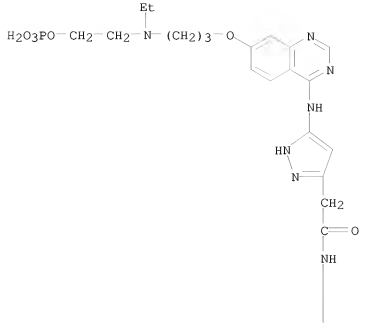

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● 2 HCl

RN 722543-53-5 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(3-fluorophenyl)-5-[[7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

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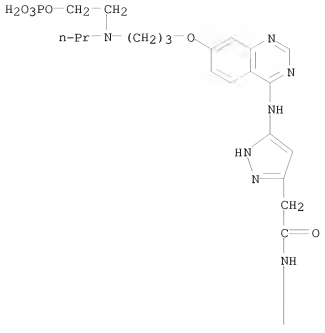

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● 2 HCl

RN 722543-56-8 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[4-[[2-(phosphonooxy)ethyl]propylamino]butoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

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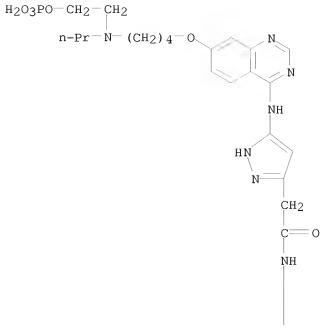

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● 2 HCl

RN 722543-57-9 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[7-[4-[ethyl[2-(phosphonooxy)ethyl]amino]butoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

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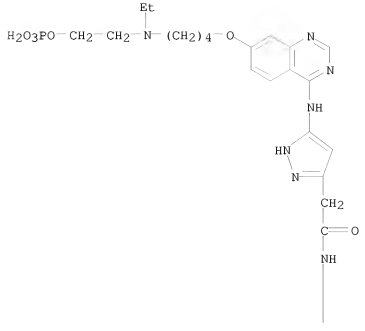

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● 2 HCl

RN 722543-62-6 CAPLUS
CN 1H-Pyrazole-3-acetamide, 5-[[7-[3-[ethyl[2-(phosphonooxy)ethyl]amino]propoxy]-6-fluoro-4-quinazolinyl]amino]-N-(3-fluorophenyl)-, hydrochloride (1:2) (CA INDEX NAME)

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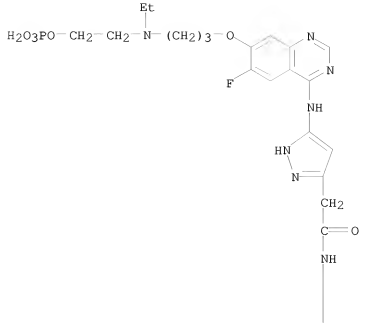

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● 2 HCl

RN 722543-78-4 CAPLUS
CN 1H-Pyrazole-3-acetamide, N-(2,3-difluorophenyl)-5-[[6-methoxy-7-[3-[[2-(phosphonooxy)ethyl]propylamino]propoxy]-4-quinazolinyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

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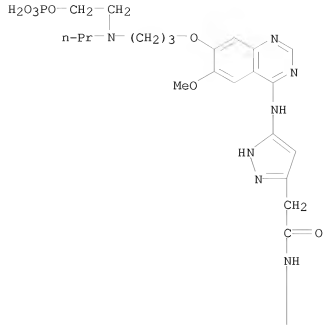

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●2 HCl

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L1             STRUCTURE UPLOADED
L2           32 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 17:14:40 ON 27 OCT 2008
L3           15 S L2

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COST IN U.S. DOLLARS                         SINCE FILE       TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                                  XXXXXXXXXXXXXXX
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.00	-12.00

STN INTERNATIONAL LOGOFF AT 17:15:14 ON 27 OCT 2008